IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION

OF: GEWEHR ET AL.

SERIAL NO. 10/616,950

FILED: JULY 11, 2003

FOR: FUNGICIDAL USE

Honorable Commissioner
for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION

I, Reinhard Stierl, Dr. agr., a citizen of the Federal Republic of Germany and residing at Jahnstr. 8, 67251 Freinsheim, Germany, hereby declare as follows:

I am fully trained agricultural engineer, having studied horticultural science at the Technical University of Munich-Weihenstephan, Germany, from 1987 to 1992;

From 1994 to 1999 I furthered my studies at the Institute of Plant Disease of the University of Bonn, and I was awarded my doctor's degree by the said university in 1999;

I joined BASF Aktiengesellschaft of 67056 Ludwigshafen, Germany, in 1998, and have since been working in the field of the characterization and screening of fungicidal substances, and am therefore fully conversant with the technical field to which the invention disclosed and claimed in application Serial No. 10/616,950 belongs.

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I have studied the record of application Serial No. 10/616,950, and particularly the Office action mailed on August 19, 2005, and the prior art applied by the Examiner, in particular the teaching of *Curtze et al.* (US 6,127,570), and the teaching of *Sieverding et al.* (US 6,696,497).

It is my understanding that the Examiner contends that the particular features of the benzophenones which are represented by formula (I) of application Serial No. 10/616,950, as well as the suitability of the compounds to control *Pseudocercosporella herpotrichoides* in crop plants which property results from the particular structure of the benzophenones of the formula (I), were already well within the purview of a person working in the field of fungicidal ingredients in view of either one of the prior art teachings referenced above.

I cannot share the Examiner's position as set forth in the Office action of August 19, 2005, for the following reasons. *Curtze et al.* specifically state that benzophenones encompassing the benzophenones of the formula I which are defined in the claims of application Serial No. 10/616,950 are effective against powdery mildew diseases like *Blumeria (Erysiphe) graminis*, *Erysiphe cichoracearum*, *Podosphaera leucotricha*, *Uncinula necator* and the like (see col. 3, lines 19 to 26, of *Curtze et al.*). It is important to note in this context that all of these pathogens grow on the leaf surfaces. In contrast thereto, the fungus *Pseudocercosporella herpotrichoides* which is referenced in the claims of application Serial No. 10/616,950 is a plant pathogen which primarily grows in the plant tissue. Further examples of pathogenous fungi which mainly grow in the plant tissue include *Alternaria solani*, *Botrytis cinerea*, *Fusarium culmorum*, *Phytophthora infestans*, *Plasmopara viticola*, *Puccinia recondita*, *Pyricularia oryzae*, or *Pyrenophora teres*.

It is well known in the fungicidal art that a large number of fungicides which are effective against powdery mildew diseases, ie. fungal diseases which grow on the surface of leaves, do not provide sufficient control of plant pathogenous fungi which mainly grow in the plant tissue. Examples of such fungicides which only provide control of powdery mildew include dinocap, bupirimate, ethirimol, dimethirimol, pyrazophos, and dodemorph.

It is also well known in the fungicidal art that the effectivity of a compound against a fungus that mainly grows in the plant tissue is influenced by a variety of factors and that not all of the factors which have an impact on the said effectivity are known or predictable. Factors which are known to be involved include lipophilicity and solubility of the compound, since these factors affect the uptake of the compound into the plant tissue. Since these factors are important for the properties of the compound within the plant tissue, they do not have a major effect on the control of fungi that live on the plant surfaces. In retrospect, it is sometimes possible to determine which factors are most likely to contribute to a found activity. However, it is frequently even then not possible to explain the activity by these factors and other factors yet unknown may play a role. Therefore it is impossible to predict the activity of compound against a plant dwelling fungus which is known to be active against powdery mildew.

The foregoing general technical background knowledge also holds true where benzophenones in general and the benzophenones of the formula I referenced in the claims of application Serial No. 10/616,950 are concerned. Benzophenones are generally known to be only poorly suited to achieve a satisfactory control of pathogenous fungi that mainly grow in the plant tissue. This is, for example, confirmed by the information available from the teaching of *Sieverding et al.* The results presented tables 1 and 2 of *Sieverding et al.* demonstrate that the benzophenone compound BP-4 (5-bromo-2',6-dimethyl-2,4',5',6'-tetramethoxy-benzophenone) exhibits, at the investigated amounts, no or only marginal effectivity against *Plasmopara viticola*, ie. a fungus which mainly grows in the tissue of the plant. The effectivity of the benzophenones I referenced in the current claims of application Serial No. 10/616,950 against *Pseudocercosporella herpotrichoides* therefore constitutes, in my opinion, an exception which could not reasonably be expected based on the information which was available from the teachings of *Curtze et al.* and of *Sieverding et al.* when the application was filed.

To further demonstrate that the efficacy of benzophenones against any particular pathogenous fungus that mainly grows in the plant tissue is even less predictable I conducted the following experiments and investigations. The tests were carried out by me or under my supervision. The tests were conducted with the compound of the following formula Ia

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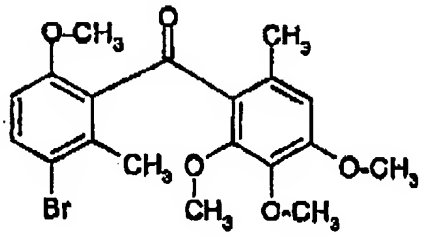

Ia

which was formulated in a stock solution as follows:

A solution of 25 mg of the benzophenone compound was extended to 10 ml with a 99:1 per volume solvent:emulsifier mixture containing acetone and/or dimethylsulfoxid as the solvent and Uniperol® EL (wetting agent having emulsifying and dispersing action based on ethoxylated alkylphenols) as the emulsifier. The 10 ml sample was further extended with water to 100 ml, and the 100 ml sample was then diluted with a mixture of the solvent, the emulsifier and water to give the desired concentration.

The efficacy of the benzophenone compound Ia against different pathogenous fungi that mainly grow in the plant tissue was investigated as follows:

Preventative fungicidal control of early blight on tomatoes (*Alternaria solani*) (ALTESO P1)

Young seedlings of tomato plants were grown in pots. These plants were sprayed to run-off with an aqueous suspension, containing 250 ppm of the benzophenone Ia. The next day, the treated plants were inoculated with an aqueous suspension of *Alternaria solani*. Then the trial plants were immediately transferred to a humid chamber. After 5 days at 20 to 22°C and a relative humidity close to 100 %, the extent of fungal attack on the leaves was visually assessed as % diseased leaf area.

Preventative control of grey mold (*Botrytis cinerea*) on green pepper (BOTRCI P1)

Young seedlings of green pepper were grown in pots to the 2 to 3 leaf stage. These plants were sprayed to run-off with an aqueous

suspension containing 250 ppm of the benzophenone Ia. The next day the treated plants were inoculated with a spore suspension of *Botrytis cinerea* in a 2 % aqueous biomalt solution. Then the trial plants were immediately transferred to a dark, humid chamber. After 5 days at 22 to 24°C and a relative humidity close to 100 % the extent of fungal attack on the leaves was visually assessed as % diseased leaf area.

Control of culm rot on pearl millet caused by *Fusarium culmorum* (FUSACU P1)

Pot-grown pearl millet seedlings with 2 - 3 true leaves of the variety "Gelbe Kolben-hirse" were sprayed to run-off with an aqueous suspension, containing 250 ppm of the benzophenone Ia. The plants were allowed to air-dry. On the following day the plants were inoculated with an spore suspension of *Fusarium culmorum* in a 2% aqueous malt solution. Then the trial plants were immediately transferred to a humid chamber. After 6 days at 23-25°C and a relative humidity close to 100 % the extent of fungal attack on the leaves was visually assessed as % diseased leaf area.

Control of late blight on tomatoes caused by *Phytophthora infestans* (PHYTIN P1)

Young seedlings of tomato plants were grown in pots. These plants were sprayed to run-off with an aqueous suspension, containing 250 ppm of the benzophenone Ia. The next day, the treated plants were inoculated with an aqueous suspension of sporangia of *Phytophthora infestans*. After inoculation, the trial plants were immediately transferred to a humid chamber. After 6 days at 18 to 20°C and a relative humidity close to 100 % the extent of fungal attack on the leaves was visually assessed as % diseased leaf area.

Fungicidal control of grape downy mildew caused by *Plasmopara viticola* (PLASVI P1)

Grape cuttings of the cultivar "Müller-Thurgau" were grown in pots to the 4 to 5 leaf stage. These plants were sprayed to run-off with an aqueous suspension, containing 250 ppm of the benzophenone Ia. The next day the treated plants were inoculated with an aqueous spore

suspension of *Plasmopara viticola* by spraying the suspension ~~is~~ at the lower leaf-side. Then the trial plants were immediately transferred for 24 h to a humid chamber with 22 - 24°C and a relative humidity close to 100 % where they were kept for 24 h. Subsequently, the plants were cultivated for a period of 5 days in a greenhouse at 20 - 25° C and a relative humidity about 50-80 %. To stimulate the outbreak of the disease symptoms, the plants were then transferred to a humid chamber again where they were kept for an additional 24 hours. Then the extent of fungal attack on the lower leaf surface was visually assessed as % diseased leaf area.

Curative control of brown rust on wheat caused by *Puccinia recondita* (PUCCRT R1)

The first two developed leaves of pot-grown wheat seedling of the variety "Kanzler" were dusted with spores of *Puccinia recondita*. To ensure the success the artificial inoculation, the plants were transferred to a humid chamber where they were kept for 24 h without light and at a relative humidity of 95 to 99 % and 20 to 22°C. The next day the plants were sprayed to run-off with an aqueous suspension, containing 250 ppm of the benzophenone Ia. The plants were allowed to air-dry. Then the trial plants were cultivated for 8 days in a greenhouse chamber at 22-26°C and a relative humidity between 70 and 80 %. The extent of fungal attack on the leaves was visually assessed as % diseased leaf area.

Preventative fungicidal control of rice blast caused by *Pyricularia oryzae* (PYRIOR P1)

Leaves of pot-grown rice seedling of the variety "Tai-Nong 67" were sprayed to run-off with an aqueous suspension containing 250 ppm of the benzophenone Ia. The plants were allowed to air-dry. On the following day the plants were inoculated with an aqueous spore suspension of *Pyricularia oryzae*. Then the trial plants were immediately transferred to a humid chamber. After 6 days at 22-24°C and a relative humidity close to 100 % the extent of fungal attack on the leaves was visually assessed as % diseased leaf area.

Control of net blotch on barley caused by *Pyrenophora teres*

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(PYRNTE P1)

The first fully developed leaves of pot grown barley plants were sprayed to run-off with an aqueous suspension, containing 250 ppm of the benzophenone Ia. The next day the treated plants were inoculated with an aqueous spore suspension of *Pyrenophora (syn. Drechslera) teres*. Then the trial plants were immediately transferred to a humid chamber. After 6 days of cultivation at 20-24°C and a relative humidity close to 100 %, the extent of fungal attack on the leaves was visually assessed as % leaf area.

The activity of the benzophenone compound Ia against *Pseudocercosporella herpotrichoides* (PSDCHE P1) in wheat plants was investigated by applying an aqueous suspension, containing 250 ppm of the benzophenone Ia to leaves of potted wheat seedlings cv. "Monopol", inoculating the treated wheat plants and assessing the extent of the development of the infection in the manner described on page 9, indicated line 35, to page 10, indicated line 2, of the application.

The results are summarized in the following table:

fungus	Fungal Attack at 250 ppm of Ia	Fungal Attack in untreated control
ALTESO P1	100 %	100 %
BOTRCI P1	100 %	100 %
FUSACU P1	90 %	90 %
PHYTIN P1	100 %	100 %
PLASVI P1	90 %	90 %
PUCCRT K1	100 %	100 %
PYRIOR P1	100 %	100 %
PYRNTE P1	100 %	100 %
PSDCHE P1	0%	90%

While powdery mildews grow mainly on the surface of plant leaves, the pathogens listed in the table above after a short infection period on the surface of the leaves (ectophytic life stage), have an endophytic growth within the plant leaves. The results demonstrate that the benzophenone Ia does not sufficiently control the short ectophytic and the following endophytic life stages and thus does not prevent the massive damage of the plants. After the short infection period

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Pseudocercosporella herpotrichoides growths deeply in the stem of cereals and in the leaf layers wrapped around the stem, thereby slowly causing a destruction of the plant tissue over a period of several weeks. During this period the fungus growing in the tissue of the stem is well protected by the leaf layers against environmental influences or direct contact with chemicals. Therefore it was highly surprising that the benzophenones I which are referenced in the claims of application Serial No. 10/616,950 and which are not active against other plant dwelling fungi provide sufficient control of *Pseudocercosporella herpotrichoides*.

I find nothing in the disclosure of either one of the references which were applied by the Examiner in the Office action dated August 19, 2005, which suggests or implies that the benzophenones I which are referenced in the claims of application Serial No. 10/616,950 are useful to control *Pseudocercosporella herpotrichoides* infections in crop plants.

I further declare that all statements made herein of my own knowledge are true and that all statements made on information or belief are believed to be true; and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 101 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Signed at 67056 Ludwigshafen, this 16th day of January 2006.

(Signature of Declarant)